

Amendments to the Specification:

Please replace the paragraph starting on page 1, line 9 with the following amended paragraph:

b1 -- Of all methods currently available for obtaining high resolution structures of biological macromolecules, NMR (nuclear magnetic resonance) is the only one that can provide this information in solution under near physiological conditions (Kremer et al., *Methods in Enzymology*; James et al., Eds.; Academic Press: San Diego, 339:3-19 (2001); Stoll et al., *Methods in Enzymology*, 182:24-38 (1990)). Even NMR structures, however, are still determined *in vitro*. Often *in vitro* buffer conditions are not selected for their closest match to the natural environment of the protein, but to optimize experimental parameters such as solubility and sensitivity, or to minimize NMR buffer signals that could interfere with the signal from the analyte of interest. --

Please replace the paragraph starting on page 11, line 18 with the following amended paragraph:

b2 -- Higher-dimensional NMR experiments can be used to measure the chemical shifts of additional types of nuclei and to eliminate problems with cross peak overlap if spectra are too crowded. In particular, the NMR method used can correlate ^1H , ^{13}C , and ^{15}N (Kay et al., J. Magn. Reson., 89:496-514 (1990); Grzesiek and Bax, J. Magn. Reson., 96:432-440 (1992)), for example in an HNCA experiment. Other heteronuclear NMR experiments can be used so long as the transfer of magnetization to all CL and protein protons is only to or from amide protons on the protein, since all carbon-attached protons in the protein are replaced with deuterons. Such experiments include HNCO, HN(CO)CA, HN(CA)CO, and CBCA(CO)NH experiments. The nomenclature of these triple resonance NMR experiments are very descriptive. The names of all nuclei which are used for magnetization transfer during the experiment are listed in the order of their use, and bracketing is used for those nuclei which are used only for transfer and whose frequencies are not detected. For example, in a HNCA experiment, magnetization starts at an amide proton (H) and is then transferred to the directly attached nitrogen atom (N) which is measured as the first spectral dimension. Then the magnetization is transferred to the C^{alpha} nucleus (CA) which is measured as the second dimension. Afterwards, the magnetization is transferred back the same way to the amide proton which is measured as the

Appl. No. 09/905,439
Amdt. dated August 26, 2003
Reply to Office Action of February 26, 2003

PATENT

B2 cond third dimension. --
